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## **Global statistics on alcohol, tobacco and illicit drug use: 2017 status report**

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**Conflict of interest declaration:** In the past 3 years, LD has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior, Mundipharma, and Seqirus. AP has received investigator-initiated untied educational grants from Mundipharma and Seqirus. SL has received investigator-initiated untied educational grants from Indivior. JG is a consultant and adviser for and has received research grants from Abbvie, Cepheid, Gilead Sciences, and Merck/MSD. He reports personal fees from Gilead, Abbvie, and MSD. RW has received fees and research grants from companies that manufacture smoking cessation medications (Pfizer, J&J and GSK). RA has received investigator-initiated untied educational grants for studies of opioid medications in from Indivior, Mundipharma, and Reckitt Benckiser. In the past 3 years, JM has received investigator-led, educational grant funding from Indivior (administered by Action-on-Addiction) for a study of personalised psychosocial intervention for non-response to opioid agonist treatment (ARC Trial) and support from NIHR (HTA) for a trial of extended-release naltrexone. He acknowledges part-time employment as Senior Academic Advisor for the Alcohol, Drugs and Tobacco Division, Health Improvement, Public Health England and consultancy to the US National Institute on Drug Abuse, Centre for Clinical Trials Network. He has received honoraria from Merck Serono (2015; clinical oncology training); Martindale (2017; expert meeting on OUD); and Indivior (via PCM Scientific) as co-chair (2015, 2016) and chair (2017) for the conference on Improving Outcomes in Treatment of Opioid Dependence. All other authors declare no competing interests.

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## Abstract

**Aims:** Alcohol, tobacco, and illicit drug use are key contributors to the global burden of disease. This aim of this review was to provide an up-to-date curated source of information on use and associated mortality and burden of disease. Limitations in the data are also discussed, including how these can be addressed in the future.

**Methods:** Online data sources were identified through expert review. Data were mainly obtained from the World Health Organization, United Nations Office on Drugs and Crime, and Institute for Health Metrics and Evaluation.

**Results:** In 2015, the estimated prevalence among the adult population was 18.3% for heavy episodic alcohol use (in the past 30 days); 15.2% for daily tobacco smoking; and 3.8%, 0.77%, 0.37%, and 0.35% for past-year cannabis, amphetamine, opioid, and cocaine use, respectively. European regions had the highest prevalence of heavy episodic alcohol use and daily tobacco use. The age-standardised prevalence of alcohol dependence was 843.2 per 100,000 people; for cannabis, opioids, amphetamines and cocaine dependence it was 259.3, 220.4, 86.0 and 52.5 per 100,000 people, respectively. High-Income North America region had among the highest rates of cannabis, opioid, and cocaine dependence. Attributable disability-adjusted life-years (DALYs) were highest for tobacco (170.9 million DALYs), followed by alcohol (85.0 million) and illicit drugs (27.8 million). Substance-attributable mortality rates were highest for tobacco (110.7 deaths per 100,000 people), followed by alcohol and illicit drugs (33.0, and 6.9 deaths per 100,000 people, respectively). Attributable age-standardised mortality rates and DALYs for alcohol and illicit drugs were highest in Eastern Europe; attributable age-standardised tobacco mortality rates and DALYs were highest in Oceania.

**Conclusions:** In 2015 alcohol and tobacco between them cost the human population more than a quarter of a billion disability-adjusted life years, with illicit drugs costing a further tens

of millions. Europeans proportionately suffered more but in absolute terms the mortality rate was greatest in low and middle income countries with large populations and where the quality of data was more limited. Better standardised and rigorous methods for data collection, collation and reporting are needed to accurately assess geographical and temporal trends in substance use and burden.

**Keywords:** alcohol; tobacco; cannabis; opioid; amphetamine; cocaine; epidemiology; prevalence; substance dependence; mortality;

## **Introduction**

Alcohol, tobacco and illicit drug use are major global risk factors for disability and premature loss of life (1). Their health burden is accompanied by significant economic costs, namely expenditure on healthcare and law enforcement, lost productivity, and other direct and indirect costs, including harm to others (2). Estimating the prevalence of use and associated burden of disease and mortality at the country, regional, and global level is critical in quantifying the extent and severity of the burden arising from substance use. This knowledge should inform allocation decisions by governments, policy-makers, and funding bodies about service provision and policy and assist in evaluations of the impact of policies (3). These estimates must be rigorously developed, regularly updated, and geographically comprehensive to quantify and detect change in indicators over time.

There are various research groups that regularly compile estimates of the global prevalence of substance use, dependence, and related disability and mortality. It is useful to collate these collections to provide an overall global picture of the distribution of substance use and associated mortality and burden of disease and to highlight key gaps in evidence. Indeed, these data are critical to monitoring progress towards Sustainable Development Goals (4), particularly those requiring quantification of the prevalence of substance use and dependence to calculate appropriate treatment and intervention coverage. This review is part of an ongoing series (5), which has two purposes, to: i) curate recent estimates of the prevalence of use, dependence, mortality and burden of disease associated with alcohol, tobacco and illicit drugs at the country, regional, and global level, and ii) comment on the availability and quality of existing data collections, and identify challenges in estimating and comparing substance use and related burden geographically and temporally. For the purpose of this review, illicit drug use was defined as use of a substance where consumption has been prohibited by

international drug control treaties except for medical purposes (3). For illicit drugs, we focused on use of cannabis (noting that policy regarding cannabis use and supply varies in some countries, e.g., USA, Netherlands; 6), methamphetamine, cocaine, as well as extra-medical opioid use (i.e., use that is without a prescription or not as directed by a doctor; 7). We also briefly considered estimates related to use of new psychoactive substances (NPS; see Box 1 for details about NPS).

## Methods

### Design

We identified online data sources on alcohol, tobacco and illicit drug use, dependence, and attributable burden of disease and mortality through web searches and email consultations with experts in the epidemiology of substance use. This review focused on data collections at the global level which also disaggregate estimates at the country and/or regional level. These collections are mainly held by the following organisations: World Health Organization (WHO); United Nations Office on Crime and Drugs (UNODC); and the Institute for Health Metrics and Evaluation's (IHME) Global Burden of Disease (GBD) study 2015. Details of data collections and reporting by these organisations (including links to downloadable data) are provided in **Table 1**, and regional classifications of countries for each organisation are provided in **Appendix A**. The below section overviews the indicators of interest, and data sources used, for the present paper. It should be noted that these organisations use different approaches for identifying source data and modelling estimates, and thus comparison of estimates from different organisations may not be valid (see Discussion for further details).

\*Table 1 approximately here\*

### *Prevalence of substance use*

Indicators of interest comprised the annual prevalence of alcohol, tobacco, and illicit drug use (including NPS and injecting drug use) amongst the adult population in 2015. Estimates of the prevalence of alcohol use for 2015 for the adult population (aged  $\geq 15$  years) by region and globally were obtained from the WHO Collaborating Centre for Addiction and Mental Health (CAMH) for validation and later inclusion into the Global Status Report on Alcohol and Health 2018 and the Global information System on Alcohol and Health (8).



Global and regional estimates of the age-standardised prevalence of daily tobacco smoking in the adult population were obtained from the GBD study 2015 (9). This indicator underestimates total prevalence in countries such as the US where non-daily smoking is relatively common but still represents substantial use. Figures on non-daily smoking were not available for many countries. This indicator also does not include non-smoked forms of tobacco (which is common in many parts of the world). Global and regional estimates of the annual prevalence of illicit drug use and NPS use amongst the adult population (age 15-64 years) in 2015 were obtained from the UNODC World Drug Report 2017 (10), with reference to European School Survey Project on Alcohol and Other Drugs 2015 report (11). Estimates of the prevalence of injecting drug use for 2015 in the adult population (age 15-64 years) were obtained from the UNODC World Drug Report 2017 (10), the GBD study 2015 (9) and from a recent multi-stage systematic review of peer-reviewed and grey literature on the global epidemiology of injecting drug use (12).

### ***Prevalence of substance dependence***

Indicators of interest comprised the prevalence of past year alcohol, tobacco, and illicit drug dependence amongst the adult population in 2015. Modelled estimates of global and regional all-age number and age-standardised rate (per 100,000 people) of past year dependence on alcohol, amphetamine, cannabis, cocaine, and opioids were obtained from the GBD study 2015 by region (9). Estimates of smoked tobacco dependence are not modelled in the GBD study. Daily smokers have very low probability of successful quitting in any given attempt (13) and so daily smoking was considered indicative of a significant level of dependence in the current study. Substance dependence was defined according to the Diagnostic and Statistical Manual of Mental Disorders IV edition (14) and the International Classification of

Diseases 9<sup>th</sup> or 10<sup>th</sup> edition (15). We used this rather than ‘substance use disorder’ as defined in DSM 5<sup>th</sup> edition because that is the most commonly available indicator globally.

### ***All-cause substance-attributable mortality***

Estimates of smoked tobacco, alcohol, and illicit drug all-cause attributable mortality from all disease and injuries were obtained from the GBD study 2015 (9). The regional and global number of all-age attributable deaths and age-standardised death rate (per 100,000) are presented.

### ***Substance-attributable burden of disease***

Disease burden caused by alcohol use, tobacco smoking, and illicit drug use as risk factors are presented. Burden of disease was presented for substance use attributable disability-adjusted life years (DALYs) which are the sum of years of life lost (YLLs) to premature mortality and years of life lived with disability (YLDs). Modelled estimates of global and regional attributable DALYs (all-ages) and age-standardised (per 100,000 people) attributable DALYs for alcohol, smoked tobacco, and illicit drugs for the adult population were obtained from the GBD study 2015 (9). We also obtained estimates of the serological prevalence of HIV and hepatitis C virus (HCV) antibody among the adult population (age 15-64 years) who inject drugs from the UNODC World Drug Report 2017 (10) and from a recent multi-stage systematic review of peer-reviewed and grey literature on the global epidemiology of injecting drug use (12).

### **Analyses**

Modelled estimates are presented as obtained from source documents. Uncertainty intervals (UI) are presented where available to indicate the uncertainty range around the estimate; the

way in which these intervals were generated differs across data collections (see details in Table notes).

## Results

### Substance use

Globally, CAMH (8) estimated that 6.42 litres of pure alcohol per capita were consumed by the adult population (aged  $\geq 15$  years) in 2015 (**Table 2**). Approximately one-fifth (18.3%) of the adult population (or two-fifths (40.3%) of all adult alcohol consumers) reported heavy episodic drinking ( $\geq 60$ g alcohol on one occasion) in the past 30 days (**Table 2; Figure 1a**). Central, Eastern, and Western Europe recorded consistently higher alcohol consumption per capita (11.61, 11.98 and 11.09 litres, respectively) and a higher percentage of heavy consumption amongst consumers (50.5%, 48.2%, and 40.2%, respectively). North Africa and the Middle East recorded the lowest alcohol consumption per capita (0.91 litres pure alcohol) and the lowest percentage of alcohol consumers who reported heavy drinking (17.3%). Central Sub-Saharan Africa showed unique findings, with the highest proportion of heavy consumption (79.7%) despite a relatively low per capita consumption (4.72 litres).

The GBD study 2015 (9) estimated that the same European regions also recorded the highest age-standardised prevalence of daily tobacco smoking (Eastern Europe 24.2% [22.7, 25.7], Central Europe 23.7% [22.6, 24.8], and Western Europe 20.9% [20.2, 21.7]), with the lowest prevalence recorded in Western Sub-Saharan Africa (4.7% [4.3, 5.1]). The European regions and Southeast Asia had a smoking prevalence that was significantly higher than the global prevalence (**Table 2; Figure 1b**). Globally, the age-standardised prevalence of daily smoking was 15.2% (14.7, 15.7). Across all ages globally, there were 933.1 (901.5, 966.5) million people who smoked tobacco daily. China (268.3 million [263.3, 273.5]), India (104.2 million [99.2, 109.6]), and Indonesia (53.7 million [49.6, 58.3]) had the largest number of smokers that together accounted for 45.7% of daily smokers globally.

\*Table 2 and Figure 1 approximately here\*

Global estimated annual prevalence of illicit drug use as reported in the UNODC World Drug Report 2017 (10) was highest for cannabis (3.8% [2.7, 4.9] of adults aged 15-64 years old), followed by amphetamines (0.77% [0.30, 1.24]), opioids (including prescription opioids and opiates; 0.37% [0.27, 0.49]), and cocaine (0.35% [0.27, 0.46]; **Table 3**). There was substantial subregional variation in prevalence, particularly for cannabis use (1.8% [1.0, 3.0] in Asia to 10.3% in Oceania [8.7, 14.7]). The UNODC World Drug Report 2017 (10) also collates estimates of NPS use. Fewer than 1% of sampled populations (typically household surveys or surveys of school students) reported use of specific NPS in the past year (see **Box 1** for discussion of limitations and future directions of monitoring NPS use).

\*Table 3 and Box 1 approximately here\*

In the UNODC World Drug Report 2017 (10) it was estimated that 0.25% (0.18, 0.36) of the adult population aged 15-64 years reported injecting drug use in 2015, equating to 11.8 million (8.6, 17.4) people (**Table 3**). In contrast, a recent global systematic review (12) estimated that 0.33% (0.21, 0.49) of the adult population reported injecting drug use in the past year in 2015. This equates to 15.6 million (10.2, 23.7) people (**Figure 2**).

\*Figure 2 approximately here\*

### Substance dependence

Globally, alcohol dependence was the most prevalent substance of dependence (**Table 4**), with 63.5 million (57.5, 69.9) estimated cases in 2015: an age-standardised rate of 843.2

(763.7, 927.3) per 100,000 people. Cannabis and opioids dependence were the most common types of illicit drug dependence, with 19.8 (18.0, 21.8) and 16.7 (14.7, 19.1) million cases in 2015 (age-standardised rates of 259.3 [235.7, 285.5] and 220.4 [193.1, 251.0] per 100,000 population), respectively. Amphetamine and cocaine dependence were less prevalent, with 6.6 million (5.3, 8.0) and 3.9 million (3.4, 4.3) cases globally in 2015 (corresponding to age-standardised rates of 86.0 [69.2, 104.6] and 52.5 [46.6, 58.7] persons per 100,000 population), respectively.

\*Table 3 approximately here\*

The high prevalence of different types of substance dependence in some regions reflected their higher prevalence of substance use. For example, the High-Income North America region (the US and Canada) had one of the most prevalent rates of cannabis, opioid, and cocaine dependence (748.7 [694.8, 812.3], 650.0 [574.5, 727.3], and 301.2 [269.3, 333.7] per 100,000 people, respectively). Australasia (Australia and New Zealand) had the highest prevalence of age-standardised rates of amphetamine dependence (491.5 per 100,000 people [441.4, 545.5]), as well as high rates of cannabis, opioid and cocaine use dependence (693.7 [648.1, 744.4], 509.9 [453.7, 577.8], and 160.5 [136.4, 187.1] per 100,000 people, respectively). Age-standardised prevalence of amphetamine, cannabis, cocaine and opioid dependence were largely lowest in Central Sub-Saharan Africa, Eastern Sub-Saharan Africa, and Western Sub-Saharan Africa. The most marked regional variation was in alcohol dependence: the highest age-standardised rate was in Eastern Europe (2786.7 [2487.3, 3109.6] per 100,000 people) and the lowest in North Africa and the Middle East (274.2 [241.7, 309.3] per 100,000 people).

### **Substance use attributable mortality and burden of disease**

Globally, the highest age-standardised rates of mortality were for smoked tobacco as a risk factor at 110.7 (101.0, 120.3) per 100,000 deaths, compared to 33.0 (28.0, 37.7), and 6.9 deaths 6.9 (6.1, 7.6) per 100,000 people in 2015 for alcohol and illicit drugs, respectively (**Table 5; Appendix B**). Alcohol and illicit drug attributable age-standardised mortality rates were highest in Eastern Europe (108.0 [63.5, 152.4] and 23.7 [21.0, 25.9] deaths per 100,000 deaths, respectively). Tobacco attributable mortality rates were highest in Oceania (which includes e.g. Papua New Guinea, Kiribati, Federated States of Micronesia, Solomon Islands; 269.3 [184.4, 382.9] deaths per 100,000 deaths).

Variations in burden of disease estimates by types of substance as risk factors largely reflected those for mortality. Absolute burden was highest for tobacco, with 170.9 million (156.2, 186.0) tobacco-attributable DALYs (see Appendix **B** for smoking and second-hand smoking attributable DALYs). This was followed by 85 million (77.2, 93.0) alcohol attributable DALYs and 27.8 million (24.4, 31.2) illicit drug attributable DALYs 2015 (**Table 4; Figure 3**). Estimates of alcohol and illicit drug attributable burden rates were highest in Eastern Europe (4,033.5 [3259.9, 4795.1] and 1,386.5 [1229.6, 1535.4] age-standardised DALYs per 100,000 population, respectively). Tobacco-attributable burden rates was highest in Oceania (7,149.7 [4888.1, 10491.5] age-standardised DALYs per 100,000 population).

\*Table 4 and Figure 3 approximately here\*

Alcohol-attributable burden was primarily due to cirrhosis (17.0 million DALYs [15.6, 18.3] all ages), transport injuries (16.8 million DALYs [14.9, 18.9]), and cancers (12.1 million

DALYs, [11.1, 12.9]) (9). Illicit drug attributable burden was concentrated in drug use disorders (16.9 million [14.0, 19.9], of which 12.9 [9.9, 14.1] were opioid use disorders-attributable), cirrhosis (4.7 million [3.8, 5.5]), HIV infection (3.0 million [2.6, 3.6]), and liver cancer (1.8 million [1.4, 2.1]) (9).

A recent global systematic review (12) estimated that there are 8.2 million (4.7-12.4) people who inject drugs who are HCV antibody positive, and that 2.8 million (1.5-4.5) people who inject drugs are living with HIV. This is equivalent to 52.3% (42.4-62.1%) and 17.8% (10.8-24.8%) of people who inject drugs globally, respectively. The UNODC World Drug Report (10) also included estimates of HCV amongst people who inject drugs (51.7%, equating to 6.1 million people, no uncertainty interval available) and of HIV among people who inject drugs (13.1%, equating to 1.6 million [0.9-3.2]).

## **Discussion**

### **Main findings**

Alcohol use and tobacco smoking are far more prevalent than illicit substance use, globally and in most regions. Global estimates suggest that one in five adults report at least one occasion of heavy episodic alcohol use in the past month, increasing their risk of acute harm (e.g., injury; 8). Nearly one in seven adults (15.2%) were estimated to engage in daily tobacco smoking, increasing their risk of 12 types of cancer, non-malignant respiratory diseases, cardiovascular disease and a wide array of other chronic health conditions (16). In contrast, use of illicit drugs was far less common. Fewer than one in twenty people were estimated to use cannabis in the past year, and much lower estimates were observed for amphetamines, opioids and cocaine.



The majority of the health burden from substance use was attributable to tobacco smoking (the most prevalent substance) and the smallest attributable to use of illicit drugs. There was substantial geographic variation in these estimates and several caveats (discussed below) need to be borne in mind when interpreting these data.

### **Data availability**

Certain countries and regions (e.g., Africa, Caribbean and Latin America, Asia regions) have limited or no data on substance use and associated health burden. These are typically low or middle income countries that frequently have punitive drug policies, and may experience serious political and social unrest. These countries often warrant enhanced monitoring because they are at risk of rapid escalation in substance use and related health burden. For example, a recent review found evidence of injecting drug use in 23 countries in Sub-Saharan Africa where it had not been previously documented (12). Yet only 7 of the 37 countries that had evidence of injecting drug use in the Sub-Saharan Africa region offered needle-syringe programmes, and only eight offered medication assisted treatment for opioid dependence. The coverage of interventions, where they were offered, was very low (17). These countries face the risk of a rapid escalation in HIV infection among people who inject drugs.

In countries where no data have been collected, an alternative is to impute prevalence.

Imputed prevalence can be based on prevalence in neighbouring countries and country-level predictors. The GBD study uses Disease Modeling – Metaregression (DisMod; 18) to fill in gaps where data are incomplete to produce prevalence and disease burden estimates for each disease cause, age group, sex, country, and year. There are, however, substantial uncertainties in these modelled estimates. This can be reduced only as better epidemiological evidence becomes available.

## Data quality and estimation

The quality of estimates is often poor when data are available. For example, there is greater geographic coverage in estimates of alcohol use because consumption can be better monitored via surveys (19), and taxation, production, import and export data are available to produce estimates of consumption (20). However, unrecorded consumption, which is estimated to account for about 25% of all alcohol use globally, introduces marked measurement error (21). Similarly, prevalence of daily tobacco smoking obtained from the GBD study 2015 did not include non-daily smoking and abstinence among those who have ever smoked (see 22 for further details of estimation of prevalence of tobacco smoking in GBD), which varies considerably across countries (23). Indeed, a review of 16 countries showed a substantially lower rate of abstinence amongst people who formerly smoked tobacco daily in China, India, Egypt, Russia and Bangladesh (<20%) relative to similar indicators in UK, USA, Brazil and Uruguay (>35%) (23). Further, the estimates of prevalence of daily tobacco smoking did not include smokeless tobacco product use, as well as the use of e-cigarettes and heat-not-burn tobacco products. Given the emerging trends of non-cigarette products, it would be useful to have these modelled separately to monitor changes in prevalence over time for different types of tobacco products in the population.

The need to measure progress towards various targets for improving global health has facilitated progress in standardising epidemiological indicators across studies (4, 24). Nonetheless, there is no gold-standard method for estimating how many people use or are dependent on alcohol, tobacco and illicit drugs, and no single method is ideal for all substances in all national contexts (**Table 6**). General population surveys rely on honest self-report of substance use. Marginalised groups with high levels of problematic substance use

(e.g. prisoners, homeless people) or those living in countries where substance use is forbidden or stigmatised for religious or cultural reasons, are often excluded from such surveys. This leads to under-estimates of the prevalence of the most stigmatized and harmful forms of substance use in way that can vary geographically (3). Indirect methods of estimating prevalence for more stigmatised forms of substance use (e.g., multiplier, capture-recapture, network scale-up) may be biased by data limitations (e.g. dependencies between data sources in capture-recapture studies; 25). Even use of multiple indirect methods to estimate a single population size may not remedy biases in individual methods, as estimates may be inconsistent with each other, and simply averaging across estimates is not guaranteed to reduce bias (26). Multiparameter evidence synthesis addresses these limitations by triangulating all available evidence (including estimates of potential biases) but this approach is complex and technically challenging to implement (27).

\*Table 6 approximately here\*

Differences in estimates also occur across data collections. For example, we reported estimates of global prevalence of injecting drug use from the UNODC World Drug Report 2017 (0.25% [0.18, 0.36]; 10) and a recent systematic review of peer-review and grey literature (0.33% [0.21, 0.49]; 12). In this instance, data sources used within each country to model prevalence were mostly the same and the uncertainty intervals overlapped, suggesting that prevalence lies somewhere within this range. Yet, the various collections are based on different search processes, criteria for source data inclusion, and modelling approaches to derive global estimates. For example, crude data included as input for analysis in the GBD study 2015 were extracted from national data systems (e.g., vital statistics, disease registries, demographic surveillance systems), surveys (e.g., household surveys), clinical informatics

(e.g., disease notification data, health service encounter data such as hospital inpatient episodes), grey literature (e.g. government / country reports, EMCDDA), and scientific literature (e.g., peer-reviewed papers containing health-related data; 28). The GBD study 2015 used Disease Modeling – Metaregression (DisMod; 18) which checks internal consistency of existing estimates and fills in gaps where data are incomplete to produce prevalence and disease burden estimates (29). The GBD study 2015 also produced UIs which capture uncertainty from sample sizes of data sources, multiple modelling steps and from sources such as model estimation and model specification (30). In contrast, the United Nations Office on Drugs and Crime (UNODC) (31) primarily derive data from the Annual Reports Questionnaire (ARQ) completed by Governments of Member States each calendar year. Estimates are computed using various adjustments, and imputation for countries where data are missing based on countries in the same subregion. Upper and lower uncertainty range estimates are calculated at a 90% confidence interval among those aged 15-64 years (see 31 for further details of methods). Yet, global estimates from these organisations cannot be combined to identify the ‘true’ prevalence. Instead we require the collection of high-quality data and interrogation of estimation methods to maximise their consistency.

\*Table 5 approximately here\*

### **Quantifying burden of disease and mortality**

There must be direct evidence that exposure to alcohol, tobacco or illicit drugs is (to some degree) linked to a health outcome before any such injury or disease is quantified within attributable burden (32). This is challenging because risk can vary according to substance type, frequency and quantity of use, route of administration, and concomitant use of substances. The quality of epidemiological data also varies across substances, with stronger evidence for the effects of alcohol and tobacco than for illicit drugs. The GBD study (9)

represents one effort to regularly review, synthesise and evaluate the weight of evidence to support attribution (wholly or in part) to use of the specific substance (see **Appendix C** for disease conditions included in attributable burden quantification in 2015).

There are a number of injury and disease categories where there is growing epidemiological evidence for causality (e.g. depression attributable to alcohol and illicit drugs; 33) and biologically plausible attribution based on the pharmacodynamics of alcohol, tobacco, and illicit drugs. These factors suggest that we underestimate the true burden of alcohol, tobacco and especially illicit drug use. The degree of underestimation will be reduced by high quality studies on the acute and chronic causal effects of substances (e.g., emergency room studies, autopsy studies and, in particular, longitudinal cohort studies with record linkage to administrative health data) and comprehensive systematic reviews of these studies that assess the relative risk for incidence of injuries and diseases.

There are also limitations in the mortality data modelled in the GBD study. Data on causes of death are dependent on the quality of death certificates, verbal autopsies, and the study's method for code reassignment to likely cause of death when deaths are assigned codes that cannot be the underlying causes of death. For example, recent US research has shown corrected opioid-related mortality counts and rates 21-35% higher than original estimates from 1999-2015 when missing data on the specific opioid underlying drug poisoning deaths were imputed (34). Future research on the validity of code redistribution methods (e.g. for drug overdose deaths) and higher quality original data (including integrating verbal autopsies with vital statistics) will improve mortality estimates (35). Further details on the limitations on the cause of death modelling method in the Global Burden of Disease study are published elsewhere (36).

It is important to acknowledge that estimates of burden quantify only the health consequences primarily for the consumer and largely omit effects on others (with some exceptions, e.g., effects of foetal alcohol exposure, second-hand smoking). They also do not quantify broader social and economic burdens imposed by substance use.

### **Measuring trends**

We did not investigate trends over time in substance use and related burden in this review, although trend analyses have been conducted in other publications (e.g., 37). The quality of trend data is considerably poorer for illicit drugs than for alcohol and tobacco consumption, where many countries have high quality epidemiological data on use and consumption data over many years.

To validly assess change in substance use and burden we need national surveillance systems that have been conducted regularly and consistently over time in their definition of indicators, data collection methods, sampling, and geographic coverage. Guidelines on epidemiological indicators (e.g., 23) and methods of measuring indicators (e.g., 38) will facilitate use of consistent approaches over time and between countries. The ability to implement regular studies are limited by the significant costs and resources needed to establish and regularly conduct surveillance studies, particularly population surveys. Improved data collection and estimation may mean that apparent temporal changes reflect variation in methods rather than ‘true’ changes in the indicator of interest.

One potentially useful new approach, particularly for illicit drug use, is to monitor levels of drug metabolites and residues in wastewater. Wastewater analyses can provide trends in total

population-level consumption of licit and illicit drugs, as indexed by a population-normalised load of drug residue within the catchment area of wastewater treatment plants (typically mg/1000 people/day; 39, 40). Direct inferences about changes in the number of people who use drugs or their patterns of use cannot be made using this data, but it may provide objective information that is not subject to underrepresentation of population groups or self-report bias as with surveys. Wastewater analysis may help identify the full spectrum of pharmacological compounds consumed, including low prevalence drugs (e.g., NPS) and substances that are unknowingly consumed (e.g., mephedrone where sold as MDMA; 40). Further, wastewater can be regularly sampled and tested in near real-time. Various surveillance systems globally (40) now include wastewater data alongside survey results and indirect statistical methods to monitor spatiotemporal trends.

### **Conclusions**

Alcohol, tobacco and illicit substance use are important contributors to global burden of morbidity and mortality. Tobacco and alcohol are more commonly used and make larger contributions to disease burden than illicit drugs, but the latter's burden is underestimated because of limitations on data availability and quality. Regular compilations of global data on geographic variations in prevalence of substance use and disease burden, such as this, may encourage the improvements in data and methods required to produce better future estimates.

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# Global Substance Use: 2017 Update

**Table 1: Primary global data collections of substance use, substance dependence, and attributable mortality and morbidity**

Organisation/Group	Assessed Substances	Assessed Indicators <sup>a</sup>	Regular Reports (frequency)	Source of Data	Recency of Data	Frequency of Data Update	Coverage of Countries	Downloadable data <sup>b</sup>	Link to Data Repository
<b>Institute for Health Metrics and Evaluation: Global Burden of Disease study 2015</b>	Alcohol, tobacco, amphetamines, cocaine, cannabis, opioids	Use, hazardous use, dependence/use disorder, mortality, DALYs, YLL, YLDs	Regular journal articles and reports	Data from publications and crude data from registries, surveillance systems, censuses, and household surveys	2016	Annual	All countries with available data identified in sources	Global Health Exchange Data: country and regional summary data	<a href="http://ghdx.healthdata.org/gbd-2015">http://ghdx.healthdata.org/gbd-2015</a>
<b>World Health Organization (WHO)</b>	Tobacco and alcohol (some measurement of illicit drug outcomes)	Use, level of use, dependence/use disorder, mortality, DALYs	World Health Statistics (annual); WHO Global Status on Alcohol and Health (every 3 to 5 years); WHO Report on the Global Tobacco Epidemic (every 2 years)	Reports by member states and data produced by other international agencies	2015 (yet can be over a decade old where new estimates not available)	Periodic	All countries (197 countries) with available data	Global Health Observatory Data Repository: country-level summary data	<a href="http://www.who.int/gho/en/">http://www.who.int/gho/en/</a>
<b>United Nations Office on Drugs and Crime (UNODC)</b>	Amphetamine, cannabis, cocaine, ecstasy, opioids, new psychoactive substances	Use, injecting drug use, HIV, HCV, HBV, TB, mortality, treatment engagement, illicit drug price, illicit drug seizures	World Drug Report (Annual)	Country Annual Report Questionnaires (ARQ) by member states and government documents	2015 (yet can be over a decade old where new estimates not available)	Annual	101 countries completed ARQ for 2015 reporting, predominantly from Europe, Asia and Americas	UNODC Statistics: country and regional summary data	<a href="https://data.unodc.org/">https://data.unodc.org/</a>

**Note.** The table lists global data sources used in the current paper; details in the above table were correct as of September 6, 2017. <sup>a</sup> Reporting on these indicators may not be available for all substances listed in the prior column. Excluding alcohol and tobacco, ‘use’ typically refers to unsanctioned use of psychoactive drugs whose possession and/or supply is illegal in most jurisdictions or prescription medications (primarily opioids) that are being used in an unsanctioned way. Hazardous/problem use varies in definition according to substance and organisation. <sup>c</sup> Downloadable data may not be available for all substances/indicators. DALYs: disability-adjusted life year; YLL: years of life lost; YLD: years lost due to disability; HCV: hepatitis C virus; HBV: hepatitis B virus; TB: tuberculosis

**Table 2: Modelled regional estimates of prevalence of alcohol use and tobacco smoking, 2015**

Region <sup>a</sup>	Alcohol consumption per capita <sup>b,c</sup> Litres (UI)	Heavy episodic drinking amongst adult population <sup>b,d</sup> % (UI)	Heavy episodic drinking amongst adult alcohol consumers <sup>b,e</sup> % (UI)	Alcohol abstinence amongst adult population <sup>b,f</sup> % (UI)			Age-standardised prevalence of daily tobacco smoking <sup>g</sup> % (UI)		
				Lifetime	Former	12 months	Males	Females	Total
Andean Latin America	5.64 (4.45, 6.84)	23.8 (19.4, 28.1)	47.1 (38.5, 55.7)	10.2 (7.4, 13.9)	39.4 (33.8, 45.8)	49.6 (41.2, 59.6)	14.5 (13, 16.2)	4.3 (3.8, 4.9)	9.4 (8.4, 10.5)
Australasia	10.47 (8.55, 12.39)	34.4 (30.2, 38.7)	43.9 (38.5, 49.3)	9.3 (7.5, 11.5)	12.3 (10.1, 14.9)	21.6 (17.6, 26.3)	15.7 (14.7, 16.6)	13.5 (12.7, 14.4)	14.6 (13.7, 15.5)
Caribbean	6.27 (5.74, 6.81)	18.3 (16.5, 20.2)	44.1 (39.6, 48.6)	33.8 (29.7, 38.3)	24.9 (20.8, 29.3)	58.7 (50.4, 67.6)	13.7 (12.4, 15.2)	5.9 (5.1, 6.9)	9.8 (8.7, 10.9)
Central Asia	4.71 (3.93, 5.48)	11.8 (10.8, 12.9)	42.8 (38.9, 46.8)	46.9 (42.9, 51)	26.2 (23.5, 29.3)	73.1 (66.3, 80.3)	26.9 (25.9, 27.9)	2.8 (2.5, 3.2)	14.5 (13.8, 15.2)
Central Europe	11.64 (10.59, 12.68)	33.1 (30.1, 36.1)	49.5 (45, 54.1)	15.3 (12.9, 18.1)	18.2 (15.8, 21)	33.5 (28.7, 39.1)	28.5 (27.6, 29.5)	19.2 (18, 20.4)	23.7 (22.6, 24.8)
Central Latin America	5.96 (5.21, 6.71)	16 (14.1, 18)	40.1 (35.3, 45)	25.9 (22.3, 29.9)	34.4 (29.6, 39.3)	60.3 (51.9, 69.2)	14.6 (13.2, 16.1)	5.4 (4.7, 6.1)	9.9 (8.9, 11)
Central Sub-Saharan Africa	4.14 (3.29, 4.98)	32.8 (30.1, 35)	78.9 (72.4, 84.3)	39.8 (34.1, 45.9)	18.9 (14.8, 23.6)	58.7 (48.8, 69.5)	13.8 (12.7, 14.9)	1.1 (0.8, 1.5)	7.4 (6.7, 8.2)
East Asia	7.14 (5.35, 8.94)	22.6 (14.2, 31.8)	41 (25.8, 57.5)	42.7 (34.5, 51.1)	2.1 (1.2, 3.5)	44.8 (35.8, 54.5)	37.1 (34.7, 39.6)	2.2 (1.5, 3.1)	20.1 (18.5, 21.8)
Eastern Europe	11.55 (9.64, 13.46)	24.3 (21.7, 26.8)	46.9 (42, 51.8)	37.4 (34.2, 40.7)	11.3 (9.9, 13)	48.7 (44.1, 53.7)	38.7 (37.1, 40.2)	12.1 (10.8, 13.6)	24.2 (22.7, 25.7)
Eastern Sub-Saharan Africa	4.75 (4.06, 5.43)	13.1 (12.1, 14.1)	47.2 (43.4, 51)	60.5 (57.2, 63.8)	13.1 (11.4, 15.1)	73.7 (68.6, 78.9)	12.5 (11.9, 13.2)	1.6 (1.5, 1.7)	7.0 (6.6, 7.4)
High-income Asia Pacific	8.42 (7.16, 9.69)	30 (25.4, 34.7)	45.9 (38.8, 53.1)	8.3 (5.5, 12.3)	26.5 (22.3, 32.2)	34.8 (27.8, 44.5)	28.6 (27.2, 30.1)	9 (8.1, 10)	18.6 (17.4, 19.8)
High-income North America	9.71 (7.92, 11.5)	25.7 (23.2, 28.2)	35.7 (32.3, 39.2)	10 (8.7, 11.5)	18.2 (16.1, 20.6)	28.2 (24.7, 32)	14.4 (13.2, 15.8)	11.8 (10.9, 12.8)	13.1 (12, 14.3)
North Africa and Middle East	0.9 (0.74, 1.05)	0.9 (0.7, 1.1)	15.4 (11.7, 19.8)	92.6 (91.3, 93.6)	2.9 (2.1, 3.9)	95.5 (93.4, 97.6)	22 (21.1, 22.9)	4.3 (3.9, 4.8)	13.4 (12.7, 14.1)
Oceania	1.49 (1.27, 1.71)	9.7 (9.1, 10.3)	63.3 (59.2, 67.2)	64.9 (61.7, 68)	19.7 (17.4, 22.2)	84.6 (79.1, 90.2)	34.5 (31.7, 37.3)	13.3 (11.6, 15.2)	24.0 (21.8, 26.4)
South Asia	4.47 (3.22, 5.73)	14 (12.4, 15.6)	39.7 (35.1, 44.4)	61.1 (56.2, 65.9)	7.2 (4, 10.9)	68.3 (60.2, 76.8)	19.5 (17.5, 21.8)	3.1 (2.4, 4.1)	11.5 (10.1, 13.2)
Southeast Asia	4.22 (3.41, 5.02)	10.3 (9.3, 11.4)	33.4 (30, 37)	49.3 (45.9, 52.7)	20.8 (19.1, 22.7)	70.1 (64.9, 75.4)	37.7 (36.4, 39.1)	3.9 (3.4, 4.5)	20.7 (19.7, 21.7)
Southern Latin America	9.71 (7.98, 11.43)	21.1 (17.4, 25)	31.4 (25.9, 37.3)	6.8 (5.3, 8.8)	26.1 (21.4, 31.4)	33 (26.7, 40.2)	23 (21.1, 25)	17 (15.7, 18.6)	19.9 (18.3, 21.7)
Southern Sub-Saharan Africa	8.39 (7.06, 9.73)	16.7 (15.3, 18)	57.4 (52.6, 62.1)	57.6 (53.2, 61.8)	13.6 (11.3, 16.3)	71.2 (64.5, 78.2)	21.4 (19.9, 22.8)	6.2 (5.1, 7.4)	13.6 (12.4, 14.9)
Tropical Latin America	8.26 (6.38, 10.14)	20.2 (16.8, 23.7)	48.3 (40, 56.5)	20.3 (14.5, 27.5)	37.8 (28.9, 47.2)	58 (43.4, 74.6)	12.6 (10.8, 14.6)	8.2 (6.6, 9.9)	10.4 (8.7, 12.2)
Western Europe	11.13 (10.46, 11.81)	30.5 (28, 32.9)	40.2 (37, 43.4)	10.7 (9.4, 12.1)	14.2 (13.3, 15.3)	24.9 (22.7, 27.3)	23.4 (22.7, 24.2)	18.5 (17.8, 19.3)	20.9 (20.2, 21.7)
Western Sub-Saharan Africa	8.4 (7.43, 9.37)	20 (18.3, 21.8)	46.2 (41.9, 50.4)	55.4 (51.9, 58.8)	4.4 (2.8, 6.2)	59.7 (54.7, 65)	7.9 (7.4, 8.4)	1.4 (1.2, 1.7)	4.7 (4.3, 5.1)
<b>Global</b>	<b>6.43 (6.22, 6.63)</b>	<b>18.4 (15.1, 21.8)</b>	<b>39.6 (32.8, 46.8)</b>	<b>44.7 (40.3, 49.3)</b>	<b>11.9 (9.6, 14.6)</b>	<b>56.6 (49.9, 63.8)</b>	<b>25.0 (24.2, 25.7)</b>	<b>5.4 (5.1, 5.7)</b>	<b>15.2 (14.7, 15.7)</b>

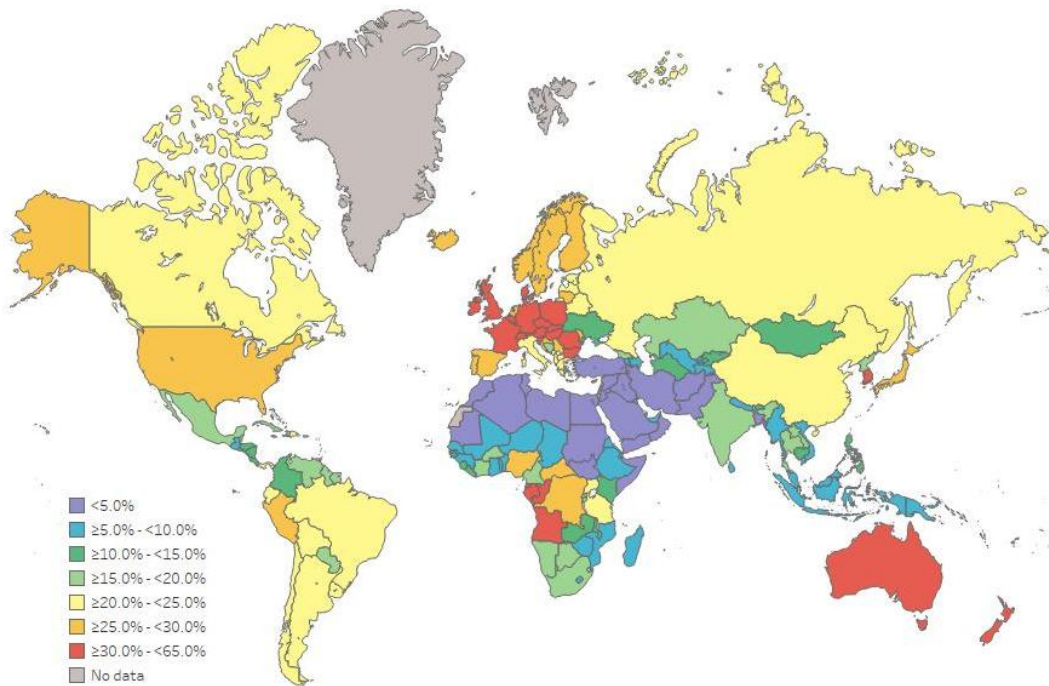
**Note.** <sup>a</sup> Grouping of countries reflect GBD classification. <sup>b</sup> Data were made available by the WHO Collaborating Centre for Addiction and Mental Health, as reported 13<sup>th</sup> November 2017, for the year 2015 by country, for validation and later inclusion into the Global Status Report on Alcohol and Health 2018 and the Global information System on Alcohol and Health (8). <sup>c</sup> Recorded APC is the recorded amount of alcohol consumed per capita (15+ years) over a calendar year in a country, in litres of pure alcohol, calculated according to the midyear resident population (15+ years) for the same calendar year according to the UN World Population Prospects. <sup>d</sup> Heavy episodic drinking is the proportion of adults (15+ years) who have had at least 60 grams or more of pure alcohol on at least one occasion in the past 30 days (computed from the total number of participants (15+ years) responding to the corresponding question(s) in the survey plus abstainers). <sup>e</sup> Heavy episodic drinking (drinkers only) is the proportion of adult drinkers



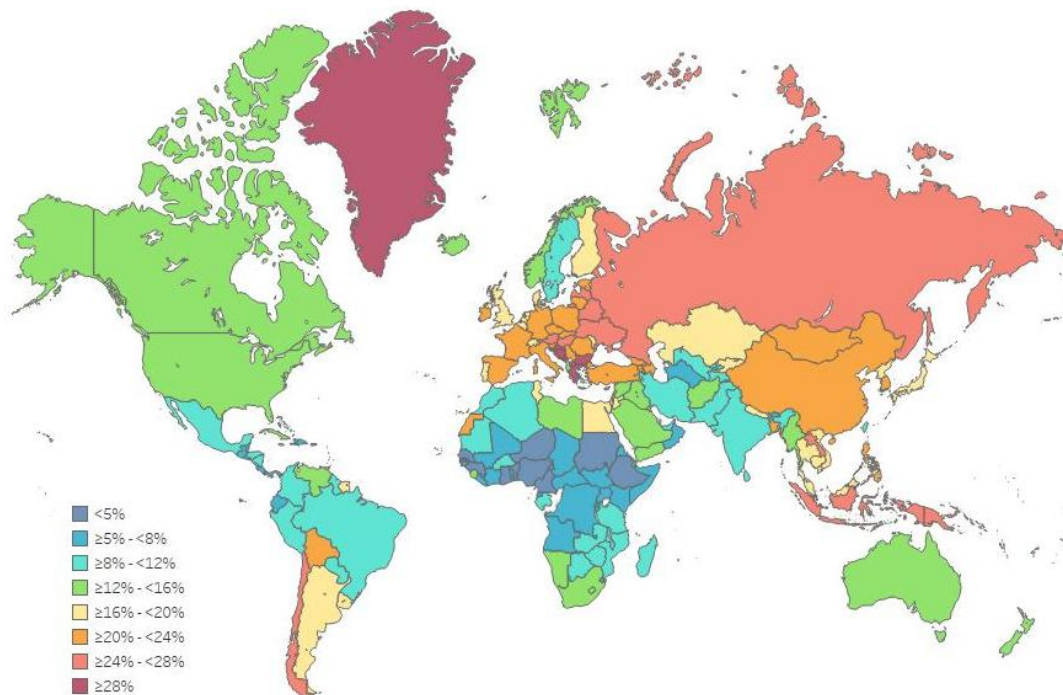
## Global Substance Use: 2017 Update

(15+ years) who have had at least 60 grams or more of pure alcohol on at least one occasion in the past 30 days (computed from the total number of respondents (15+ years, appropriately weighted) to the corresponding survey question(s) who reported having consumed an alcoholic standard drink (10 grams) within the past 12 months on the same survey (or 1-abstainers)).<sup>f</sup> Lifetime and past 12 month abstainers are the proportion of adults (15+ years) in a given population who have not consumed any alcohol during their lifetime or past 12 months, respectively, assessed at a given point in time (computed from the total number of participants (15+ years) responding to the corresponding question in a given survey). Former drinkers is the proportion of adults (15+ years) in a given population who did not consume alcohol in the last 12 months, but who did previously do that, assessed at any given point in time (computed from the total number of participants (15+ years) responding to the corresponding question in a given survey).<sup>g</sup> Data on daily tobacco smoking were extracted from the GBD study 2015 (9). Age-standardised rates is the rate per 100,000 people, estimated using the GBD world population age standard. In the GBD study, 95% uncertainty intervals (UIs) are derived from 1000 draws from the posterior distribution of each step in the estimation process. The UIs capture uncertainty from multiple modelling steps and from sources such as model estimation and model specification.

**Figure 1: Annual prevalence of heavy episodic alcohol use (total population 10+ years old; Panel A) and daily tobacco smoking (age-standardised; Panel B), by country, 2015**



**Panel 1A. Heavy episodic alcohol use**



**Panel 1B. Daily tobacco smoking**

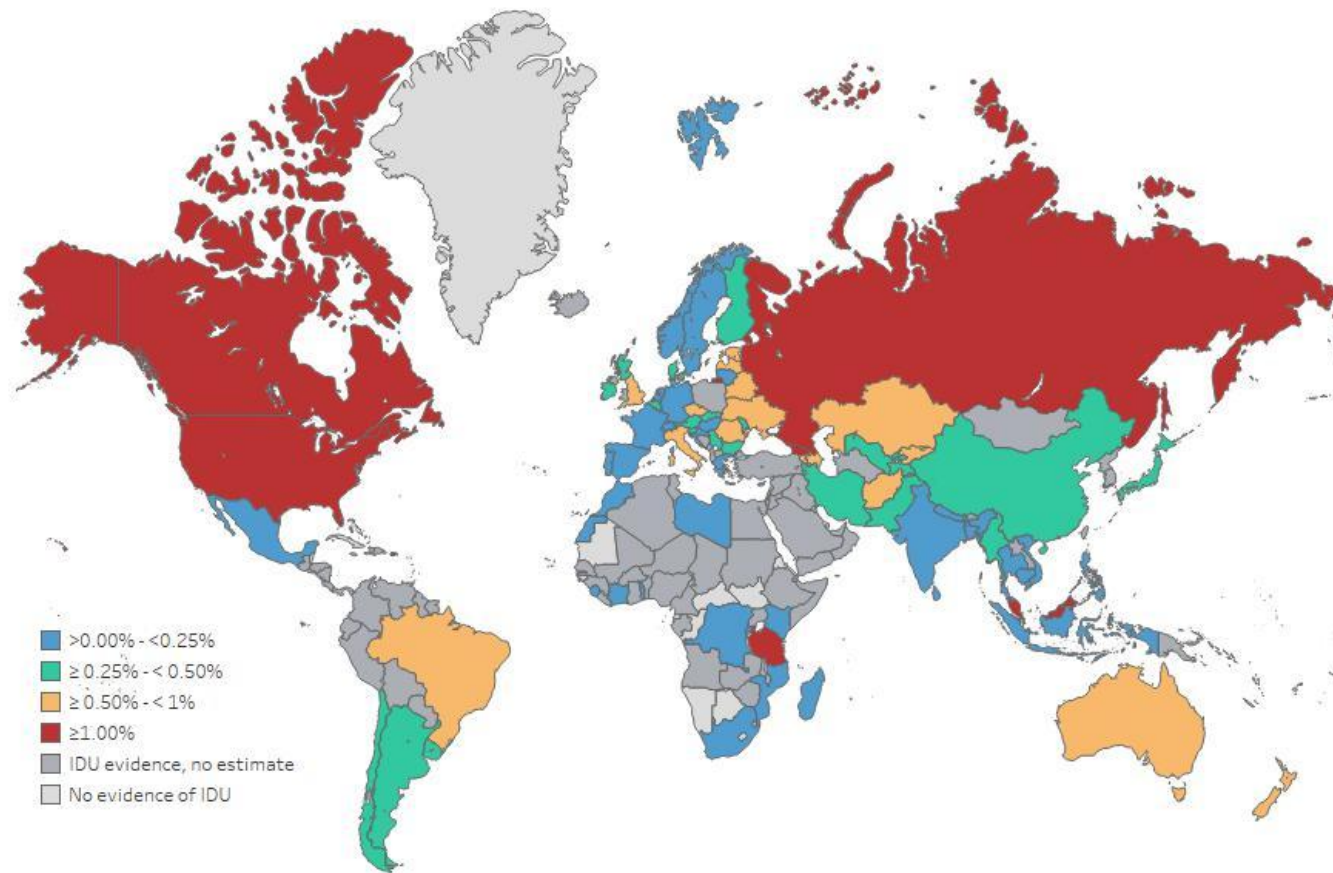
**Note.** Alcohol estimates were made available by the WHO Collaborating Centre for Addiction and Mental Health; tobacco smoking estimates were made available from the GBD study 2015 (9).

**Table 3: Past 12 month prevalence of any drug use among the population aged 15-64 years, by region and globally, 2015**

Region/Subregion <sup>a</sup>	Amphetamine <sup>b</sup> % (Lower, Upper)	Cannabis % (Lower, Upper)	Cocaine <sup>c</sup> % (Lower, Upper)	Opioids <sup>d</sup> % (Lower, Upper)	Injecting drug use % (Lower, Upper)
Africa	0.90 (0.23, 1.54)	7.5 (3.2, 9.8)	0.43 (0.13, 0.78)	0.30 (0.14, 0.39)	0.10 (0.05, 0.33)
East Africa	-	-	-	-	~
North Africa	0.58 (0.20, 0.98)	4.3 (1.7, 7.1)	0.02 (0.01, 0.02)	0.24 (0.08, 0.43)	~
Southern Africa	-	-	-	-	~
West and Central Africa	-	12.4 (5.1, 13.3)	0.69 (0.24, 1.05)	-	~
Americas	1.13 (0.95, 1.33)	7.5 (7.3, 7.8)	1.29 (1.18, 1.38)	0.27 (0.23, 0.36)	0.42 (0.44, 0.57)
Caribbean	0.86 (0.05, 1.91)	2.1 (0.8, 7)	0.62 (0.18, 1.23)	0.15 (0.07, 0.48)	0.21 (0.11, 0.39)
Central America	0.71 (0.52, 0.95)	-	0.61 (0.38, 0.83)	-	~
North America	1.97 (1.69, 2.26)	12.4 (12.3, 12.4)	1.77 (1.73, 1.80)	0.47 (0.43, 0.50)	0.65 (0.56, 0.75)
South America	0.25 (0.24, 0.26)	2.9 (2.8, 3.0)	0.88 (0.75, 0.96)	0.06 (0.03, 0.21)	~
Asia	0.70 (0.15, 1.26)	1.8 (1.0, 3.0)	0.04 (0.01, 0.08)	0.37 (0.25, 0.52)	0.16 (0.12, 0.20)
Central Asia	-	-	-	0.90 (0.80, 1.00)	0.79 (0.71, 0.90)
East and South-East Asia	-	-	-	0.20 (0.15, 0.31)	0.20 (0.14, 0.26)
Near and Middle East/ South-West Asia	0.31 (0.20, 0.55)	2.7 (1.9, 3.9)	-	1.40 (0.83, 2.14)	0.07 (0.02, 0.12)
South Asia	-	-	-	-	0.03 (0.03, 0.03)
Europe	0.45 (0.36, 0.59)	5.2 (5.0, 5.4)	0.74 (0.65, 0.98)	0.57 (0.54, 0.60)	0.65 (0.45, 0.99)
Eastern and South-Eastern Europe	0.32 (0.18, 0.56)	2.4 (2.2, 2.5)	0.27 (0.13, 0.72)	0.85 (0.82, 0.88)	1.25 (0.79, 2.04)
Western and Central Europe	0.55 (0.48, 0.62)	7.2 (7.0, 7.4)	1.08 (1.02, 1.16)	0.37 (0.34, 0.41)	0.22 (0.20, 0.25)
Oceania	1.91 (1.51, 2.08)	10.3 (8.7, 14.7)	1.54 (1.54, 1.89)	0.10 (0.10, 0.17)	0.61 (0.47, 0.75)
<b>Global</b>	<b>0.77 (0.30, 1.24)</b>	<b>3.8 (2.7, 4.9)</b>	<b>0.35 (0.27, 0.46)</b>	<b>0.37 (0.27, 0.49)</b>	<b>0.25 (0.18, 0.36)</b>

**Note.** Data in the table above were extracted from the ‘Maps and Tables’ of the UNODC World Drug Report 2017 (10), and estimates here were as reported by UNODC on September 6, 2017. The annual prevalence rate is defined as the number of people who have consumed the drug at least once in the 12 months prior to the study, expressed as a percentage of the population aged 15-64, as provided by the United Nations Population Division for the year 2015. Estimates refer to unsanctioned use; that is where possession and/or supply is illegal or prescription medications are being used in an unsanctioned way. Estimates are derived from country-level annual report questionnaire data and other official sources. Subregional estimates are computed where prevalence estimates for at least two countries covering at least 20% of the population were available; - denotes that an estimate was not available. Uncertainty ranges were calculated using UNODC’s regional and global estimation methods, taking the 10<sup>th</sup> percentile of the lower bounds of the uncertainty ranges and the 90<sup>th</sup> percentile of the upper bounds of the uncertainty ranges, based on the 90% confidence intervals or best available estimates available for countries with data within the regions (see 31 for further details of calculation uncertainty ranges). <sup>a</sup> Grouping of countries reflect United Nations Statistics Divisions, showing regions (bold) and within these sub/intermediate regions, noting that some intermediate regions are clustered (e.g., West and Central Africa). <sup>b</sup> Amphetamines include both amphetamine and methamphetamine. <sup>c</sup> Cocaine includes cocaine salt, "crack" cocaine and other types such as coca paste, cocaine base, basuco, paco and merla. <sup>d</sup> Opioids includes prescription opioids and opiates (including heroin and opium).

**Figure 2: Estimated prevalence of injecting drug use (IDU) by country, 2015**



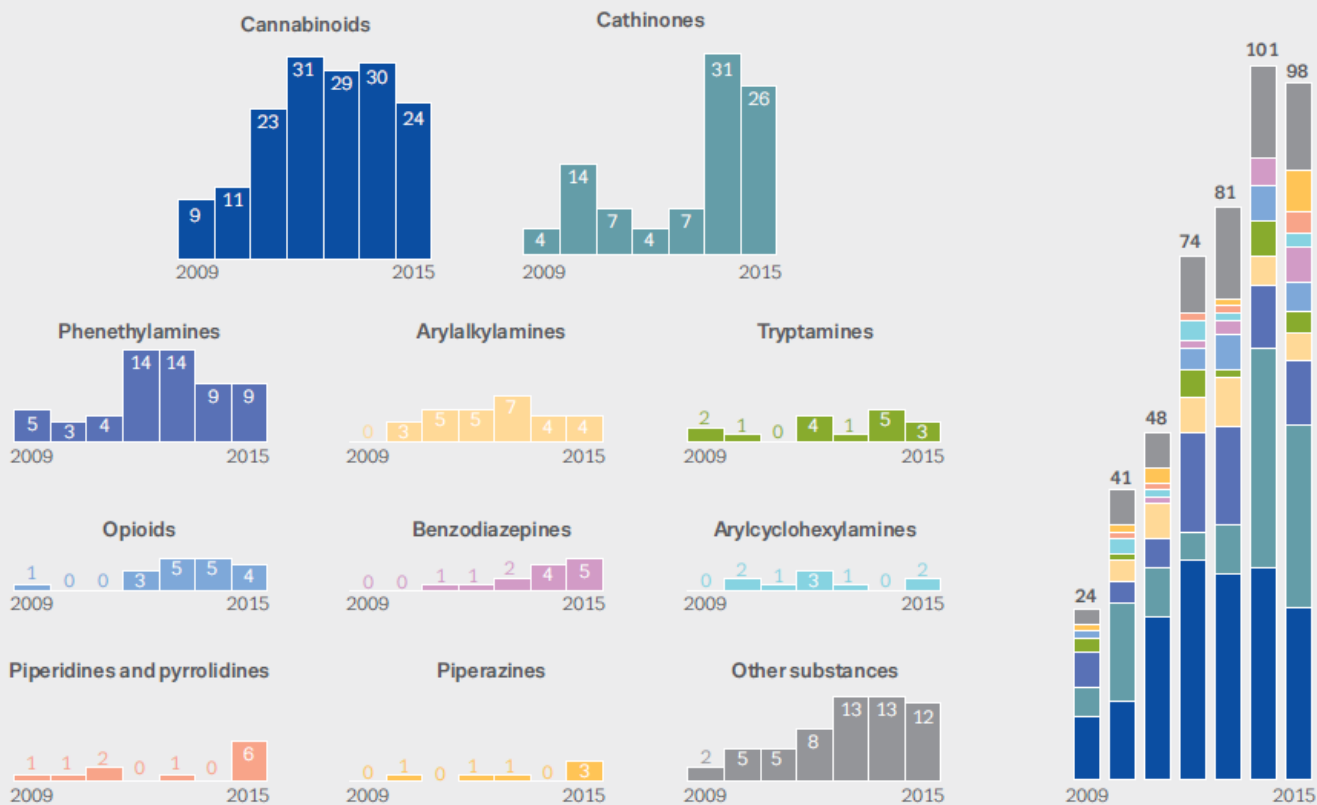
**Note.** Data are derived from a global review of the prevalence of recent ( $\leq 12$  month) injecting drug use among those aged 15-64 years old based on UN population division estimates of country size in 2015 (see 12 for full details of estimation methods). Image reproduced here from (12).

**Box 1: Monitoring new psychoactive substance (NPS) use and harms**

- New psychoactive substances (NPS) are substances which have similar acute psychoactive effects to established illicit drugs but are not controlled under international drug controls (41).
- There has been a growth in the number of NPS notified to the EU early warning system for the first time (see figure below), although the rate growth in 2016 declined (42).
- This expanding production makes monitoring prevalence of NPS use challenging and there are substantial gaps in knowledge about the extent of NPS use. The UNODC World Drug Report 2017 (10) listed estimates of prevalence of NPS use for only 15 countries since 2006.
- UNODC's country-level estimates of past year NPS use (10) are typically <1% of the sampled population. They are mainly derived from adolescent and young adult samples and are typically specific to a NPS class (e.g., piperazines) or substance (e.g., mephedrone) (10).
- Higher rates have been reported from the European School Survey Project on Alcohol and Other Drugs 2015 (11), with 3% of 15-16 year old European school students reporting any NPS use at least once in the past 12 months, with higher prevalence in Estonia and Poland (8%).
- Reported prevalence may be low amongst the general population but needs to be considered in the context of considerable epidemiological challenges in this area which include problems with the definition of NPS and a lack of standardized measurement tools.
- Indeed, self-report data are becoming less reliable for assessing drug groups like NPS where consumers may be unaware or misinformed of the substance they have consumed. Various indicators can be monitored and triangulated to better quantify NPS use and associated harms (e.g. ambulance attendances, emergency department presentations, poisons and toxicology data, and law enforcement drug seizures; 43).
- Key to monitoring NPS is early detection of NPS entering the market which have the capacity to cause substantial harm to the consumers, as illustrated by the recent emergence of highly potent synthetic opioids (42).
- Although NPS comprise a minority of the drugs for sale, surface and darknet websites (44) for this purpose, yielding timely and regular data on changes in the NPS market.

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Number and categories of new psychoactive substances notified to the EU Early Warning System for the first time, 2009–15



Number and categories of new psychoactive substances notified to the EU Early Warning System for the first time, 2009-2015 (adapted from 42, 43)

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**Table 4: Modelled estimates of cases and age-standardised rates of past year substance dependence by GBD region, 2015**

Region <sup>a</sup>	Alcohol		Amphetamines		Cannabis		Cocaine		Opioids	
	Number (95% UI)	Age SDR (95% UI)	Number (95% UI)	Age SDR (95% UI)	Number (95% UI)	Age SDR (95% UI)	Number (95% UI)	Age SDR (95% UI)	Number (95% UI)	Age SDR (95% UI)
Andean Latin America	494,000 (416,000, 570,000)	864.3 (729.3, 989.9)	67,000 (52,000, 85,000)	104.7 (82.0, 132.2)	118,000 (104,000, 132,000)	187.8 (166.3, 210.4)	56,000 (49,000, 65,000)	101.1 (88.1, 114.9)	86,000 (74,000, 101,000)	149.2 (127.8, 173.4)
Australasia	326,000 (292,000, 364,000)	1065.5 (950.8, 1203.5)	138,000 (124,000, 153,000)	491.5 (441.4, 545.5)	195,000 (182,000, 208,000)	693.7 (648.1, 744.4)	47,000 (40,000, 54,000)	160.6 (136.4, 187.1)	152,000 (135,000, 171,000)	509.9 (453.7, 577.8)
Caribbean	657,000 (589,000, 731,000)	1430.1 (1285.7, 1589.6)	7,000 (5,000, 8,000)	14.4 (10.9, 18.2)	127,000 (112,000, 142,000)	271.6 (239.9, 305.0)	34,000 (29,000, 39,000)	74.4 (62.9, 86.3)	57,000 (49,000, 66,000)	124.5 (107.0, 144.2)
Central Asia	1,028,000 (908,000, 1,163,000)	1138.7 (1011.3, 1276.8)	65,000 (51,000, 82,000)	67.1 (52.9, 83.1)	284,000 (251,000, 321,000)	300.4 (266.8, 338.2)	27,000 (22,000, 31,000)	30.2 (25.5, 34.9)	183,000 (157,000, 214,000)	196.7 (168.7, 228.4)
Central Europe	1,491,000 (1,334,000, 1,653,000)	1112.1 (992.8, 1237.6)	135,000 (111,000, 161,000)	127.7 (104.0, 154.5)	344,000 (315,000, 376,000)	324.8 (295.3, 356.5)	61,000 (54,000, 69,000)	48.7 (42.0, 55.7)	213,000 (186,000, 244,000)	168.6 (145.8, 195.5)
Central Latin America	2,694,000 (2,401,000, 3,003,000)	1067.2 (957.2, 1181.6)	164,000 (126,000, 205,000)	58.8 (45.5, 73.2)	406,000 (373,000, 442,000)	148.5 (136.7, 161.4)	218,000 (187,000, 250,000)	86.8 (75.5, 98.6)	349,000 (304,000, 401,000)	135.3 (118.2, 154.3)
Central Sub-Saharan Africa	687,000 (600,000, 782,000)	796.6 (704.0, 897.4)	4,000 (3,000, 5,000)	3.5 (2.6, 4.7)	171,000 (149,000, 199,000)	160.2 (142.0, 183.9)	9,000 (7,000, 11,000)	10.8 (9.0, 12.7)	81,000 (67,000, 97,000)	89.9 (75.4, 106.2)
East Asia	13,933,000 (12,723,000, 15,154,000)	839.4 (766.2, 916.4)	2,964,000 (2,350,000, 3,624,000)	205.3 (161.5, 252.9)	4,784,000 (4,280,000, 5,338,000)	330.6 (293.4, 371.2)	729,000 (633,000, 819,000)	48.2 (41.7, 54.4)	3,037,000 (2,677,000, 3,435,000)	183.5 (161.5, 207.7)
Eastern Europe	6,845,000 (6,131,000, 7,585,000)	2786.7 (2487.3, 3109.6)	546,000 (444,000, 658,000)	259.7 (209.5, 313.7)	578,000 (522,000, 641,000)	294.2 (262.6, 328.7)	198,000 (168,000, 230,000)	86.4 (71.9, 102.2)	1,424,000 (1,233,000, 1,653,000)	583.7 (504.0, 680.6)
Eastern Sub-Saharan Africa	2,435,000 (2,124,000, 2,775,000)	815.6 (720.7, 915.9)	5,000 (3,000, 7,000)	1.3 (0.9, 1.8)	651,000 (550,000, 779,000)	175.6 (151.7, 204.6)	10,000 (7,000, 12,000)	3.8 (3.1, 4.6)	161,000 (136,000, 192,000)	53.7 (45.8, 63.1)
High-income Asia Pacific	960,000 (881,000, 1,046,000)	500.5 (453.6, 549.8)	88,000 (71,000, 108,000)	58.8 (45.9, 72.7)	565,000 (522,000, 613,000)	379.1 (348.1, 414.8)	60,000 (53,000, 68,000)	26.8 (23.1, 30.4)	198,000 (175,000, 224,000)	104.4 (91.4, 119.4)
High-income North America	4,435,000 (4,039,000, 4,852,000)	1186.4 (1075.2, 1305.5)	503,000 (418,000, 599,000)	148.4 (122.0, 177.3)	2,510,000 (2,342,000, 2,705,000)	748.7 (694.8, 812.3)	1,116,000 (1,002,000, 1,229,000)	301.2 (269.3, 333.7)	2,362,000 (2,094,000, 2,634,000)	650.0 (574.5, 727.3)
North Africa & Middle East	1,530,000 (1,335,000, 1,740,000)	274.2 (241.7, 309.3)	139,000 (108,000, 174,000)	22.7 (17.8, 28.1)	1,008,000 (876,000, 1,168,000)	164.1 (143.7, 188.5)	92,000 (76,000, 108,000)	18.3 (15.5, 21.0)	2,691,000 (2,310,000, 3,141,000)	479.3 (412.8, 555.1)
Oceania	56,000 (49,000, 63,000)	548.9 (482.5, 618.2)	5,000 (4,000, 6,000)	40.4 (29.9, 51.9)	46,000 (41,000, 53,000)	388.3 (345.5, 440.1)	1,000 (1,000, 1,000)	12.4 (10.0, 14.9)	9,000 (7,000, 10,000)	83.5 (70.4, 98.2)
South Asia	13,085,000 (11,558,000, 14,679,000)	785.7 (700.6, 873.7)	220,000 (165,000, 287,000)	11.9 (9.1, 15.4)	3,213,000 (2,896,000, 3,584,000)	173.2 (156.9, 192.4)	468,000 (385,000, 552,000)	28.9 (24.2, 33.4)	3,015,000 (2,603,000, 3,475,000)	175.7 (153.3, 200.8)
Southeast Asia	3,902,000 (3,474,000, 4,374,000)	579.8 (517.3, 647.2)	824,000 (636,000, 1,046,000)	117.3 (90.6, 148.9)	1,986,000 (1,652,000, 2,341,000)	284.4 (237.1, 334.7)	83,000 (70,000, 98,000)	13.6 (11.6, 15.8)	697,000 (591,000, 816,000)	102.1 (86.8, 118.9)
Southern Latin America	811,000 (729,000, 897,000)	1215.3 (1091.1, 1343.8)	85,000 (66,000, 106,000)	130.4 (101.2, 162.2)	227,000 (203,000, 254,000)	348.2 (312.2, 389.7)	29,000 (25,000, 33,000)	42.7 (37.4, 48.3)	124,000 (107,000, 143,000)	186.1 (160.0, 214.8)
Southern Sub-Saharan Africa	670,000 (592,000, 756,000)	945.1 (841.7, 1056.3)	18,000 (14,000, 23,000)	20.9 (16.4, 25.9)	167,000 (153,000, 183,000)	188.5 (172.9, 206.2)	18,000 (16,000, 21,000)	28.8 (25.0, 32.7)	159,000 (136,000, 186,000)	193.2 (167.3, 223.2)
Tropical Latin America	1,426,000 (1,284,000, 1,570,000)	617.3 (558.3, 676.6)	201,000 (155,000, 254,000)	87.2 (67.2, 110.4)	385,000 (352,000, 419,000)	167.0 (152.5, 181.6)	125,000 (107,000, 144,000)	57.0 (49.1, 65.2)	275,000 (241,000, 313,000)	119.3 (104.8, 135.8)
Western Europe	4,152,000 (3,792,000, 4,496,000)	880.7 (794.5, 965.0)	409,000 (342,000, 483,000)	112.1 (91.9, 134.3)	1,528,000 (1,432,000, 1,634,000)	424.9 (395.8, 456.0)	435,000 (388,000, 489,000)	103.4 (90.2, 118.2)	991,000 (865,000, 1,123,000)	233.4 (203.5, 265.6)
Western Sub-Saharan Africa	1,852,000 (1,617,000, 2,136,000)	584.4 (515.5, 661.9)	12,000 (9,000, 16,000)	3.6 (2.8, 4.6)	472,000 (413,000, 542,000)	127.0 (112.5, 143.4)	31,000 (25,000, 37,000)	12.2 (10.4, 14.2)	482,000 (401,000, 575,000)	153.3 (129.3, 179.9)
<b>Global</b>	<b>63,469,000 (57,508,000, 69,864,000)</b>	<b>843.2 (763.7, 927.3)</b>	<b>6,600,000 (5,296,000, 8,024,000)</b>	<b>86.0 (69.2, 104.6)</b>	<b>19,762,000 (17,982,000, 21,770,000)</b>	<b>259.3 (235.7, 285.5)</b>	<b>3,846,000 (3,402,000, 4,310,000)</b>	<b>52.5 (46.6, 58.7)</b>	<b>16,746,000 (14,659,000, 19,107,000)</b>	<b>220.4 (193.1, 251.0)</b>

**Note.** Data in the table above were extracted from the GBD study 2015 (9). Age-standardised rates (Age SDR) is the rate per 100,000 people, estimated using the GBD world population age standard. Substance dependence was defined according to the Diagnostic and Statistical Manual of Mental Disorders (14) and the International Classification of Diseases (15). Data are derived from systematic review of peer-review and grey literature, including estimates from studies published since 1980, and data were modelled using DisMod-MR 2.1. 95% uncertainty intervals (UIs) were derived from 1000 draws from the posterior distribution in the estimation process. Data were available for 180 countries for alcohol dependence, 55 countries for amphetamine dependence, 151 countries for cannabis dependence, 43 countries for cocaine dependence and 32 studies for

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opioid dependence. In the GBD study, 95% uncertainty intervals (UIs) are derived from 1000 draws from the posterior distribution of each step in the estimation process. The UIs capture uncertainty from multiple modelling steps and from sources such as model estimation and model specification. <sup>a</sup> Grouping of countries reflect GBD classification.



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**Table 5: Crude attributable DALYs and deaths (in 1000s) and age-standardised attributable DALYs and death rate (per 100,000) for alcohol, tobacco and illicit drugs as risk factors for disease burden by GBD region, 2015**

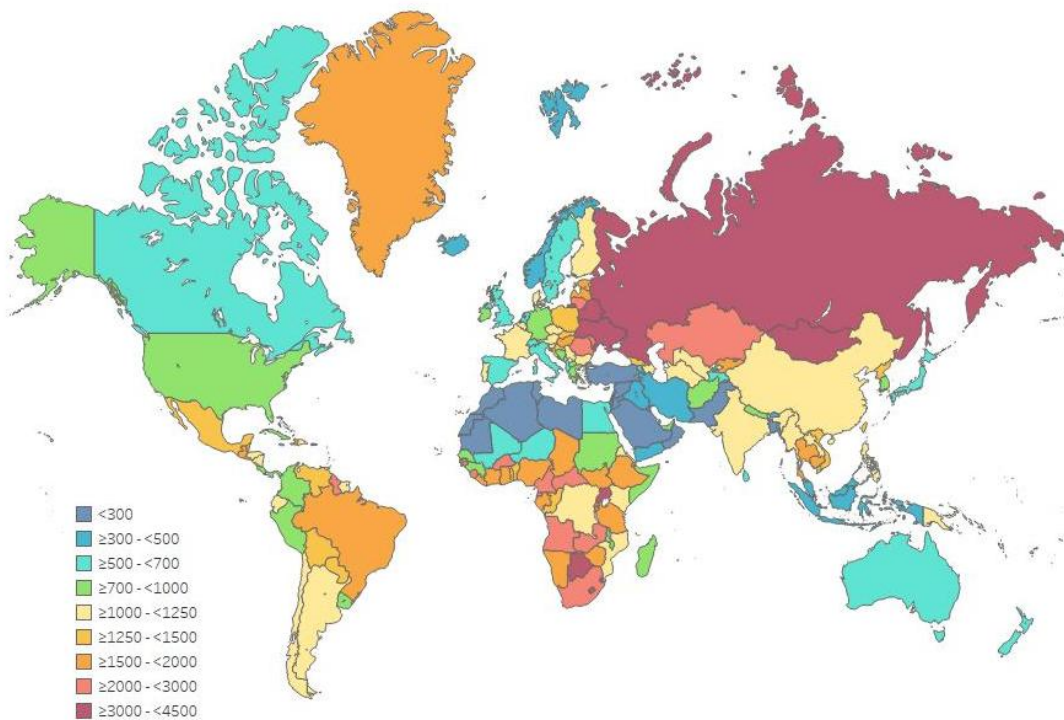
Region <sup>a</sup>	Alcohol use				Tobacco smoking				Illicit drug use			
	DALYs		Deaths		DALYs		Deaths		DALYs		Deaths	
	Number (1000s; 95% UI)	Age SDR (per 100,000; 95% UI)	Number (1000s; 95% UI)	Age SDR (per 100,000; 95% UI)	Number (1000s; 95% UI)	Age SDR (per 100,000; 95% UI)	Number (1000s; 95% UI)	Age SDR (per 100,000; 95% UI)	Number (1000s; 95% UI)	Age SDR (per 100,000; 95% UI)	Number (1000s; 95% UI)	Age SDR (per 100,000; 95% UI)
Andean Latin America	504.1 (451.4, 560.9)	951.3 (847.7, 1057.9)	13.4 (11.8, 15)	28.3 (24.7, 31.9)	394.6 (345.8, 450.9)	861 (755, 982.6)	18.2 (15.8, 20.9)	43.9 (37.9, 50.3)	135.8 (112.4, 160.8)	245.3 (202.7, 290.2)	2.1 (1.6, 2.6)	4.4 (3.4, 5.5)
Australasia	192.2 (170, 214.7)	610.4 (552.1, 678.8)	4.1 (2.2, 5.7)	12.7 (8.9, 16)	472.9 (443.8, 501.8)	1230.2 (1154.2, 1305.9)	27.3 (25.7, 29.1)	64.8 (61, 68.8)	205.2 (172.5, 240.5)	684.5 (571, 805.5)	2.6 (2.3, 2.8)	7.6 (6.8, 8.4)
Caribbean	519.8 (462.5, 582.6)	1140.2 (1013.1, 1277.2)	12.8 (11.1, 14.6)	28.7 (24.8, 32.7)	815.8 (755, 881.8)	1854.5 (1716, 2004.9)	38.6 (35.7, 42.1)	89 (82.4, 96.9)	90.6 (76.4, 105.9)	197.9 (166.7, 231.3)	1.6 (1.2, 2)	3.5 (2.7, 4.4)
Central Asia	1211.7 (1069.7, 1349.1)	1427.5 (1250.3, 1605.6)	27.9 (23.8, 32)	36.2 (29.6, 42.4)	2288.1 (2105.7, 2473)	3166.8 (2913.7, 3421.3)	80.3 (73.6, 87.1)	125.3 (114.2, 136.4)	454.9 (404.2, 506.7)	531.9 (472.2, 591.2)	9.2 (8, 10.2)	12.1 (10.3, 13.7)
Central Europe	2052.4 (1910.3, 2214.8)	1386.9 (1297.1, 1490.1)	60 (52.8, 67)	37.2 (33.4, 40.7)	4909.7 (4665.5, 5165.2)	2843 (2700.1, 2991.9)	214.6 (203.6, 225.9)	117.3 (111.4, 123.3)	395.9 (332.9, 465.7)	296.5 (250.7, 346.5)	7.8 (5.9, 9.7)	5 (3.9, 6.1)
Central Latin America	2864.7 (2673.2, 3069.3)	1186.4 (1105.4, 1274.5)	70.2 (64.5, 76)	32.6 (29.6, 35.8)	2002 (1810, 2189.8)	1021.9 (924.2, 1115)	90.7 (82, 98.9)	51.6 (46.6, 56.4)	761.6 (655.7, 862.7)	318.9 (272.2, 363.6)	15.5 (12.2, 18.5)	7.4 (5.6, 9)
Central Sub-Saharan Africa	1041.6 (641.4, 1688.4)	1506.2 (915.6, 2448.6)	25.5 (15.1, 41.8)	46.5 (27.8, 74.5)	1617.7 (1069.9, 2488.4)	2300.7 (1457.6, 3599.6)	42 (26.8, 65.3)	85.6 (53.7, 134.2)	185.1 (132, 266.7)	240.9 (167.1, 353.5)	3.4 (2.2, 5.3)	5.5 (3.4, 8.7)
East Asia	20447.6 (18657.8, 22411.1)	1221.4 (1113.4, 1339.8)	613.5 (557.7, 672)	38.5 (34.7, 42.6)	43148.3 (33306.3, 54375.7)	2730.4 (2097.5, 3428.8)	2045.2 (1542.5, 2588.2)	145.9 (109.4, 184.6)	5070.5 (4355.2, 5786.7)	312.3 (266.8, 359.2)	89.6 (81.4, 97.7)	5.6 (5, 6.1)
Eastern Europe	10749.3 (8326.4, 13121.1)	4033.5 (3259.9, 4795.1)	313.9 (164.9, 462.2)	108 (63.5, 152.4)	11323.8 (10524.6, 12139.6)	3743.6 (3478.2, 4010.6)	451.7 (417.7, 487.2)	142.8 (132.2, 154)	3364.8 (2991.3, 3716.6)	1386.5 (1229.6, 1535.4)	61.3 (54.2, 66.7)	23.7 (21, 25.9)
Eastern Sub-Saharan Africa	3656.5 (2900.3, 4619)	1629.5 (1289.5, 2063.6)	92.3 (71.9, 117.5)	52.6 (40.8, 66.6)	3891.8 (3032.5, 4928.9)	1700 (1321.8, 2184.3)	102.7 (80.1, 131.1)	63 (49.3, 81.2)	530.7 (422.6, 654.2)	198.7 (152.8, 252.9)	9.7 (7.3, 12.8)	4.5 (3.2, 6.2)
High-income Asia Pacific	1463 (1300.6, 1643)	627 (569.2, 696.6)	51.4 (43.8, 60)	17.7 (15.7, 19.9)	3485.5 (3186.8, 3762.5)	1038 (943.8, 1125.6)	221.9 (203.4, 238.8)	54 (49.6, 58.2)	521.5 (420.1, 622.6)	216.4 (180.2, 250.7)	17.1 (11.9, 22.7)	5.3 (3.9, 6.7)
High-income North America	3498.9 (3215.9, 3787.4)	880.8 (813.8, 951.1)	84.7 (74.6, 94.7)	19.6 (17.6, 21.5)	10603.2 (10143.2, 11073.7)	2141.7 (2047, 2238.8)	529.5 (508.8, 550.3)	101.2 (97.4, 104.9)	3943.1 (3506.1, 4370.8)	1032 (911.3, 1150.2)	70.7 (65.9, 74)	16.4 (15.3, 17.2)
North Africa and Middle East	1685.8 (1459.1, 1909.4)	359.3 (306.5, 407.3)	46 (39.5, 52.3)	12.3 (10.5, 14.1)	9497.9 (8615.4, 10434.8)	2339.3 (2125.8, 2554.1)	321.7 (292.7, 351.2)	94.8 (86.4, 104.1)	2122.1 (1703.9, 2564.5)	395.1 (318.9, 478.9)	23.8 (18.8, 29.4)	5.5 (4.3, 7)
Oceania	85.1 (59.1, 123.9)	903.8 (625.5, 1318.8)	1.9 (1.2, 2.8)	24.2 (16.2, 35.3)	523.1 (353.9, 779.1)	7149.7 (4888.1, 10491.5)	16 (10.7, 23.7)	269.3 (184.4, 382.9)	16.6 (12.7, 22.2)	168.4 (127.2, 226.5)	0.2 (0.2, 0.4)	3 (2, 4.4)
South Asia	15654.9 (14027.2, 17410.4)	1038.8 (928.1, 1158.3)	382.8 (336.5, 426.8)	29.4 (25.6, 33)	35866.4 (31925.8, 39858.3)	2812.6 (2508.1, 3122.3)	1263.6 (1123.6, 1396.5)	116.9 (103.4, 129.7)	3730.1 (3174.5, 4343)	222.2 (190.1, 257.4)	50.7 (44.3, 59.4)	3.5 (3, 4)
Southeast Asia	5988.3 (5255.8, 6834.3)	971.7 (854.2, 1102.7)	163.7 (141.5, 187.8)	30.7 (26.4, 34.9)	18138.8 (15949.6, 20408.4)	3361.3 (2971.9, 3764)	673.9 (599.3, 753.3)	147.6 (131.7, 164.1)	2130.2 (1740.6, 2649.9)	321.8 (263.3, 399.6)	40.5 (31.3, 52.7)	6.7 (5.2, 8.6)
Southern Latin America	700.6 (611.5, 787.9)	1047.4 (918, 1176.8)	17.5 (13.2, 21.5)	25.7 (20, 31.1)	1412.4 (1334.9, 1496.1)	2030.9 (1915.8, 2150.6)	70.4 (66, 74.9)	96.8 (91, 102.8)	231.6 (200.6, 263.6)	344.3 (298, 392.5)	5.2 (4.5, 5.8)	7.5 (6.5, 8.4)
Southern Sub-Saharan Africa	1683.9 (1470.3, 1920.4)	2436.4 (2109.6, 2805.6)	39.5 (34.1, 45.6)	68.4 (57.9, 79.6)	1854.7 (1616.7, 2154.9)	3660.4 (3215.4, 4224.6)	68.3 (59.9, 78.7)	155.9 (137.3, 177.8)	340.3 (293.8, 424.6)	443.8 (383.9, 545.2)	5.2 (4.5, 6.7)	7.7 (6.6, 9.7)
Tropical Latin America	3505.7 (3276.6, 3755.6)	1561.7 (1456.8, 1672.1)	84.3 (78.2, 90.1)	39.8 (36.8, 42.8)	3800.6 (3523.4, 4101.4)	1931.5 (1792.8, 2080.1)	166.2 (154.2, 178.2)	93.9 (87, 100.8)	477.8 (401.4, 547.5)	211.8 (177.2, 243.6)	7.9 (6.3, 9.4)	3.8 (2.9, 4.6)
Western Europe	4084.1 (3633, 4554.3)	769.6 (691, 848.8)	112.9 (87.8, 137.3)	18.8 (15.9, 21.5)	11282.6 (10706.8, 11851.6)	1626.6 (1542.1, 1709.8)	632.1 (600.3, 663.6)	77.6 (73.9, 81.2)	1817 (1588.1, 2049.7)	382.2 (330.5, 431.7)	42.8 (35.7, 49.2)	6.7 (5.8, 7.5)

### Global Substance Use: 2017 Update

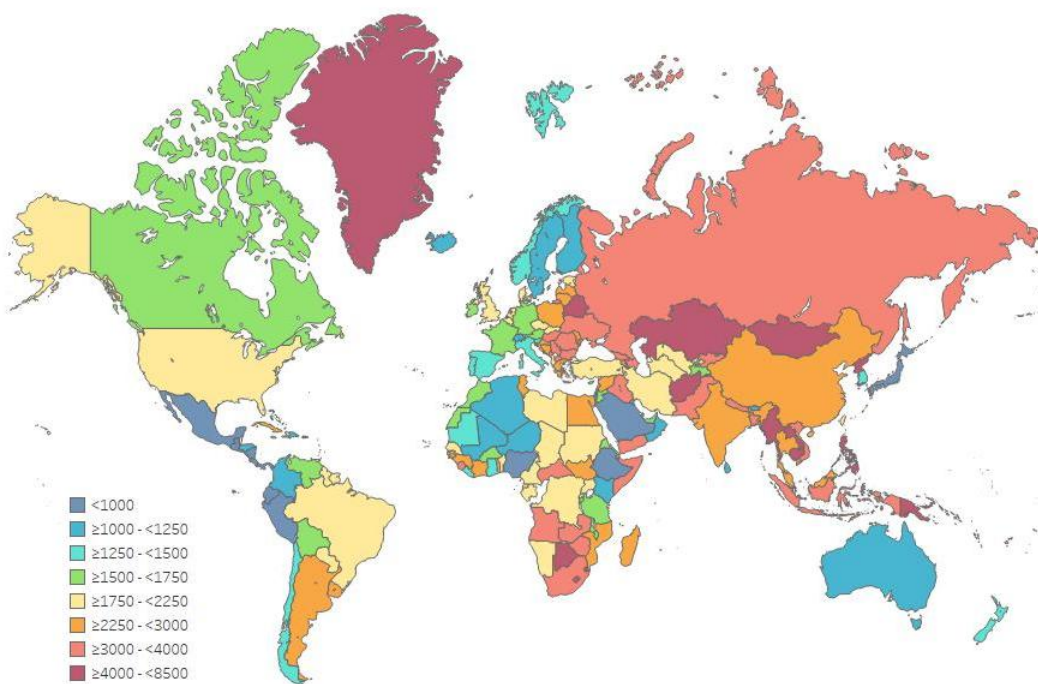
Western Sub-Saharan Africa	3400 (2779, 4468.7)	1498.9 (1215.5, 1961.9)	88.4 (70.4, 117.6)	50.8 (40.9, 66.5)	3558.7 (2787.4, 4480.4)	1405.8 (1141.2, 1772.9)	89.4 (71.7, 113)	54.5 (44, 69)	1305.7 (1046.1, 1637.8)	422 (338.5, 525.2)	21.8 (16.9, 28.2)	8.4 (6.5, 10.9)
<b>Global</b>	<b>84990 (77180.3, 93009.8)</b>	<b>1160 (1050, 1272.1)</b>	<b>2306.5 (1985.5, 2608.5)</b>	<b>33 (28, 37.7)</b>	<b>170888.6 (156215.6, 185987.6)</b>	<b>2482.8 (2269.7, 2701.2)</b>	<b>7164.5 (6544.2, 7774.8)</b>	<b>110.7 (101, 120.3)</b>	<b>27831 (24436.9, 31170.9)</b>	<b>372.1 (327.2, 416.3)</b>	<b>488.8 (439.2, 537.3)</b>	<b>6.9 (6.1, 7.6)</b>

**Note.** Data in the table above were extracted from the GBD study 2015 related to disability-adjusted life years (DALYs) and deaths attributable to substance use disorders (9). Age-standardised rates is the rate per 100,000 people, estimated using the GBD world population age standard. Data are derived from systematic review of peer-review and grey literature, including estimates from studies published since 1980, and data were modelled using DisMod-MR 2.1. 95% uncertainty intervals (UIs) were derived from 1000 draws from the posterior distribution in the estimation process. In GBD, 95% uncertainty intervals (UIs) are derived from 1000 draws from the posterior distribution of each step in the estimation process. The UIs capture uncertainty from multiple modelling steps and from sources such as model estimation and model specification. Uncertainty associated with estimation of mortality and YLLs reflects sample sizes of data sources, adjustment and standardisation methods applied to data, parameter uncertainty in model estimation, and uncertainty within all-cause and cause-specific mortality models. For estimation of prevalence and YLDs, UIs incorporated variability from sample sizes within data sources, adjustments to data to account for non-reference definitions, parameter uncertainty in model estimation, and uncertainty associated with establishment of disability weights (30). <sup>a</sup> Grouping of countries reflect GBD classification.

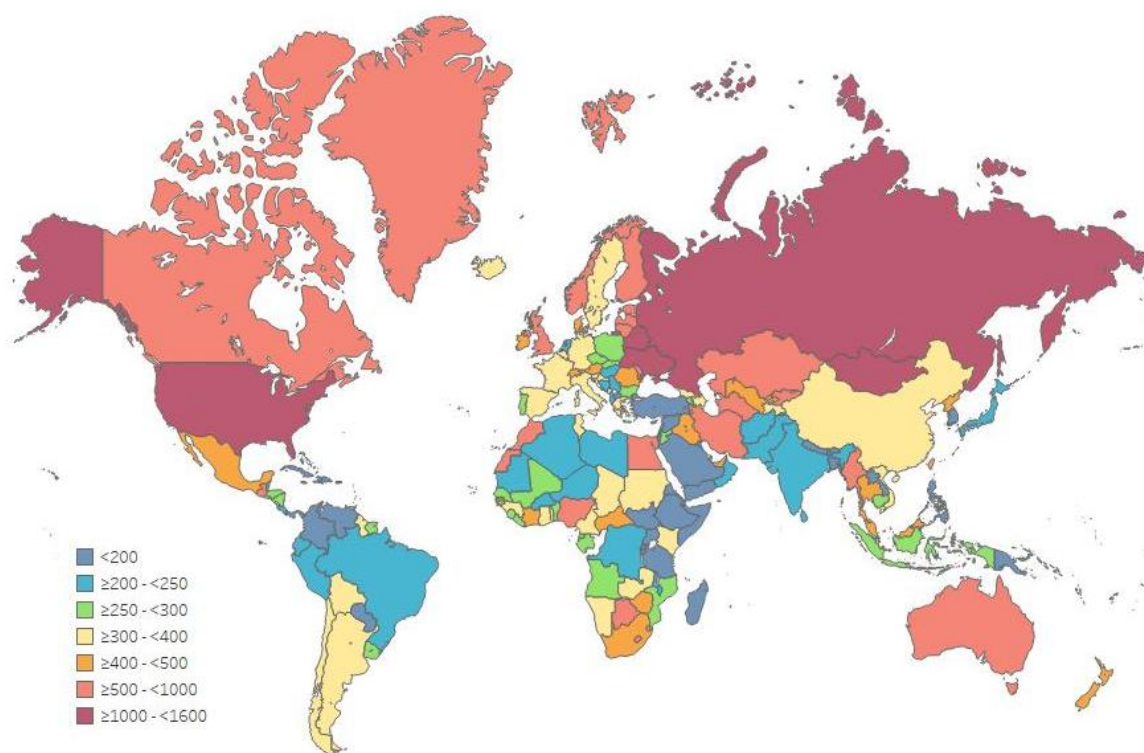
**Figure 3: Map showing distribution of alcohol (a) tobacco smoking (b) and illicit drug (c) use attributable DALYs (age-standardised rate per 100,000 population) by country in 2015**



**Panel 3a. Alcohol**



**Panel 3b. Tobacco smoking**



**Panel 3c. Illicit Drugs**

**Note.** Estimates were made available from the GBD study 2015 (9).

**Table 6: Estimating the size of the population that uses drugs**

Method	Summary	Limitations
Population surveys	Representative sample is directly asked about drug use in a specified time period.	Participants may be reluctant to disclose drug use due to illegality, stigma or concerns about confidentiality. Typically exclude groups with high levels of problematic drug use e.g. prisoners; homeless people (3).
Multiplier	A benchmark (e.g. number of people receiving drug treatment in a year) is adjusted by a multiplier (e.g. proportion of people who use drugs who report receiving drug treatment in a year) to give a population size estimate.	Data used to generate multiplier may not be representative of the population of people who use drugs, giving a multiplier that is too small or too large (45).
Capture-recapture	Population size is modelled based on the proportion of the population that is identified within more than one data source	Data sources may not be independent; e.g. criminal justice agencies may refer individuals to treatment agencies. This violates assumption of independence of capture-recapture models (25).
Network scale-up	Population size is modelled based on reports from participants in general population samples on the number of people in the target population who are in their personal social network.	Assumes that participants are aware of their social contacts being members of the target population and that members of the target population have a personal network of the same size as the general population (27).
Multiple parameter evidence synthesis	Bayesian synthesis of all available evidence, including potential biases affecting such evidence, to give an estimate that is consistent with all evidence and internally validated.	Complex relative to other methods and technically difficult to implement (27).